

THE UNIVERSITY OF CHICAGO.

(Founded by John D. Rockefeller.)

THE ACTION OF SODIUM ETHYL- ATE ON AMIDE BROMIDES

A DISSERTATION SUBMITTED TO THE FACULTIES OF THE
GRADUATE SCHOOLS OF ARTS, LITERATURE AND SCI-
ENCE IN CANDIDACY FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

Department of Chemistry

—BY—

SAMUEL ELLIS SWARTZ

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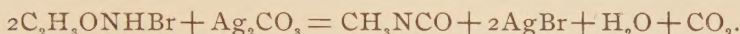
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THE ACTION OF SODIUM ETHYLATE ON AMIDE BROMIDES.

In 1881-2 A. W. Hofmann¹ developed a method for the formation of amines from acid amide bromides by treatment with caustic alkali, and proved that, in the course of the reaction, an isocyanate is first formed, which, by treatment with silver carbonate, he was able to isolate :



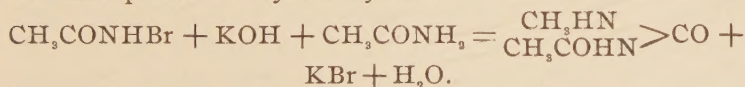
Hoogewerf and Van Dorp² improved the conditions of the reaction by using potassium hypobromite, and pointed out that the peculiar rearrangement which takes place in the molecule is perfectly analogous to the so-called Beckmann's rearrangement of ketoximes:



so also



The resulting bromformamides lose hydrobromic acid when treated with silver carbonate; with potassic hydrate they yield potassic carbonates (RNHCOOK), which Hoogewerf and Van Dorp were able to isolate in many cases, and which by saponification or treatment with acids yield amines. In the presence of an acid amide, the isocyanate or bromformamide unites with it, forming an acyl urea. For instance, acetamide bromide with potassic hydrate and acetamide gives as a final product acetyl methylurea.³



Lengfeld and Stieglitz have shown that when paranitrobenz-

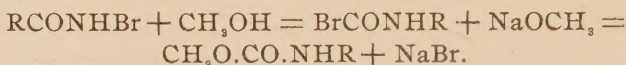
¹ Ber. d. chem. Ges., **14**, 2725; **15**, 407, 725, 762.

² Rec. Trav. Chim., **9**, 33; **10**, 4.

³ Ber. d. chem. Ges., **14**, 2725.

amide bromide¹ or succinimide bromide is acted upon by sodium methylate, a similar arrangement is effected, giving urethanes by the action of methyl alcohol on isocyanates.

Work done in this laboratory by Mr. O. K. Folin² has shown, that, in general, when other amide bromides are treated with sodium methylate in methyl alcohol solution an analogous change takes place.



In no instance has the bromine been directly replaced by the oxymethyl group.

Since molecular rearrangement of acid amide bromides is effected by a methyl alcohol solution of sodium methylate as well as by an aqueous solution of sodium hydroxide, and since, in these solutions, these substances not only exist as such but also are, to a greater or less extent, ionized, it was thought not impossible that by diminishing the electrolytic dissociation the rearrangement might be prevented and direct substitution effected.

At the suggestion of Drs. Lengfeld and Stieglitz the study of this question was undertaken by me. Dry succinimide bromide was treated with dry sodium methylate with and without a diluent, and, since ethyl alcohol causes a far smaller degree of electrolytic dissociation than methyl alcohol, various amide bromides which were found to suffer rearrangement in methyl alcohol were treated with a solution of sodium ethylate in ethyl alcohol.

It was found that succinimide bromide, treated with dry sodium methylate, regenerated succinimide, that no rearrangement took place, and that, at the same time bromine was not replaced by the methoxy group (CH_3O), but that the imido bromide was saponified or reduced, regenerating succinimide: with sodium ethylate in ethyl alcohol, in every case rearrangement was effected, and in no instance was any derivative of hydroxylamine obtained. The results obtained were perfectly analogous to those of Lengfeld and Stieglitz,

¹ Am. Chem. J., **15**, 215, 504; **16**, 307.

² The results will be published in the Am. Chem. J. for May, 1897.

and O. K. Folin, by the action of sodium methylate in methyl alcohol.

EXPERIMENTAL PART.

I. *The Action of Dry Sodium Methylate on Succinimide Bromide.*

Succinimide bromide, prepared according to the method described by Lengfeld and Stieglitz,¹ was dried for six days on clay plates over sulphuric acid in a vacuum desiccator, and the substance then carefully pulverized in a dry mortar. Sodium methylate was prepared immediately before using from absolute methyl alcohol, and was freed from alcohol in the usual way. The benzene was dried over sodium for four days and distilled.

Five grams of succinimide bromide and 1.6 grams of sodium methylate with 25 cc. benzene were heated in a sealed tube at 100° for two hours. On opening the tube a considerable quantity of gas escaped. The tube contained a dark red liquid, in which the odor of pyrrol was strong, and some undissolved material. The solution was neutral. Testing a portion with a hydrochloric acid solution of potassium iodide, there was no coloration, which indicated that no unchanged imide bromide remained. The contents of the tube were then extracted with hot benzene from which, on cooling, crystals were obtained which from their crystal form, solubility, and melting-point (125°) were identified as succinimide. The mother-liquor was then evaporated to dryness, and taken up with ether, and the colored solution digested with bone-black when the color disappeared. Ligroïn now precipitated more succinimide, and on distilling the ligroïn-ether solution a slight residue of almost pure succinimide remained. Washing the residue, insoluble in hot benzene, with water, there was obtained on evaporation the theoretical quantity of sodium bromide. While there remained insoluble in water and hot alcohol a tarry mass which amounted to almost 50 per cent. of the organic matter engaged in the reaction.

When 10 grams of succinimide bromide and 3.2 grams of sodium methylate in 100 cc. of benzene were heated under a

¹ Am. Chem. J., 15, 217.

reversed condenser the reaction was complete in four hours, no succinimide bromide remaining. The solution, which was a dark red, had a strong odor of pyrrol. Treated as above, it was found to contain about 70 per cent. of the theoretical amount of succinimide, and considerable tar, but no urethane or substituted hydroxylamine.

An attempt was made to study the effect of sodium methylate without a diluent on succinimide bromide, but the result was far from satisfactory, for when molecular quantities of the methylate and imide bromide were shaken together the action was explosively violent. When the imide bromide was added in small quantities, chemical change took place with somewhat less violence but was still very energetic. There resulted a black semi-charred mass with the odor of pyrrol, which, treated as above, yielded succinimide amounting to about 20 per cent. of the theoretical quantity, but no other organic substances could be isolated.

II. *The Action of Sodium Ethylate on Benzamide Bromide.*

To a solution of sodium ethylate prepared from 1.5 grams of sodium in 60 grams of absolute ethyl alcohol, cooled in ice water, 12.8 grams of well dried benzamide bromide were added. Reaction began slowly, as was indicated by a gradual rise in temperature. Heated on a water-bath connected with a reversed condenser, well dried and closed with a calcium chloride tube, the solution became brownish red, and after twenty minutes, a test with acidulated potassic iodide showed that the action was complete. On cooling, a heavy precipitate appeared. The slightly alkaline solution was acidulated with a few drops of dilute acid, and then filtered. Washing the precipitate with cold water to remove the sodium bromide, and recrystallizing from hot alcohol, a substance was obtained in long white needles, melting at 199° . Subjected to dry distillation, the substance gave phenyl isocyanate, which was recognized by its odor, and benzamide (melting-point 128°). These decomposition-products, the melting-point 199° , the crystal form and solubility, together with the analysis, identify it as phenyl benzoyl urea described by Kühn.¹

¹ Ber. d. chem. Ges., 17, 288r.

On analysis 0.2078 gram gave 21.6 cc. nitrogen at 18° and 742 mm. pressure.

Nitrogen	Calculated for	Found.
	$C_{14}H_{12}N_2O_2$.	
	11.66	11.77

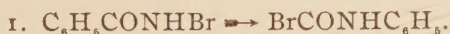
The alcoholic solution was evaporated to dryness on the water-bath and the solid residue extracted with chloroform, and dried over calcium chloride. The oil which remained was distilled under a pressure of 14–24 mm. It separated into two fractions which came over between 90°–120° and 140°–160°. The first fraction was a liquid which had a strong odor of phenyl isocyanate, and crystallized with difficulty, after standing four days. This was dried on clay plates and recrystallized from ligroin, when a constant melting-point of 52° was obtained. This, together with its boiling-point, 238° (750 mm.), identified the product as phenylurethane.

The higher fraction was a solid with a strong odor of benzonitrile. Recrystallizing from hot benzene, crystals were obtained which proved to be benzamide (melting-point 128°). Evidently some phenyl benzoylurea remained with the oil, and on distillation it decomposed, yielding phenyl isocyanate, obtained with the urethane, and benzamide, which in turn, gave a little benzonitrile.

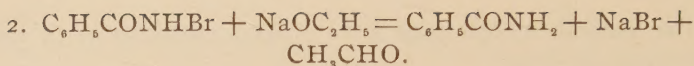
The yield was: Phenyl benzoylurea, 53 per cent.; phenylurethane, 15 per cent.; benzamide, 18 per cent. of the theoretical.

Repetition of the experiment varying the conditions of temperature and concentration of the alcoholic solution resulted in only a slight variation in the relative amounts of the products.

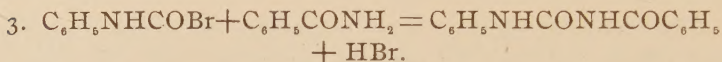
Sodium ethylate in alcoholic solution evidently acts in two ways on benzamide bromide. On the one hand, it causes a rearrangement of a part of the benzamide bromide to bromformanilide in the manner indicated above:



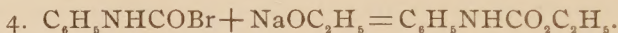
On the other hand, it reduces the benzamide bromide to benzamide, since the odor of acetaldehyde was very prominent during the reaction:



The bromformamide then unites to a large extent with the benzamide, forming phenyl benzoyl urea : ¹



and to some extent with sodium ethylate still present, giving phenyl urethane :



From the yield it was found that 45-55 per cent. of the benzamide bromide had suffered rearrangement, giving phenyl benzoyl urea and phenyl urethane.

III. *The Action of Sodium Ethylate on Paranitrobenzamide Bromide.*

Paranitrobenzamide bromide, prepared after the method of Hoogewerf and Van Dorp, is very difficult to wash and dry, and as potassium hydrate or water even in minute quantities furthers ionization, great care was taken to wash out all the caustic potash. The substance was then put on clay plates and dried in the open air for 24 hours, then pulverized and dried for six days in a vacuum-desiccator over sulphuric acid.

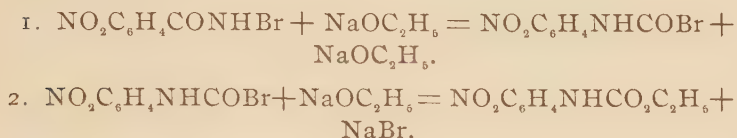
To a well cooled solution of one gram of sodium in 100 grams of absolute alcohol, 10.5 grams of *p*-nitrobenzamide bromide were added. Reaction began slowly at the temperature of the room, and heat was necessary to complete the change. After heating on a water-bath for twenty minutes, the contents of the flask needed only a drop of dilute acetic acid to render it slightly acid. Distilling off the alcohol and extracting the residue with absolute ether, a slightly yellow solution was obtained, which on cooling in a freezing-mixture, readily yielded a precipitate of yellow needles, which, after recrystallization from ligroïn, melted at 128°. This corresponded with paranitrophenyl urethane, prepared by Häger.² To identify the product more definitely, the urethane was prepared synthetically from chlorcarbonic ether and paranitranil-

¹ Ber. d. chem. Ges., 14, 2725.

² Ber. d. chem. Ges., 17, 2625.

line. It proved to be identical in color, crystal form, solubility and melting-point, with the body above described.

The action of sodium ethylate in alcoholic solution on paranitrobenzamide bromide, causes a rearrangement, yielding a urethane similar to that produced when it reacts with benzamide bromide :



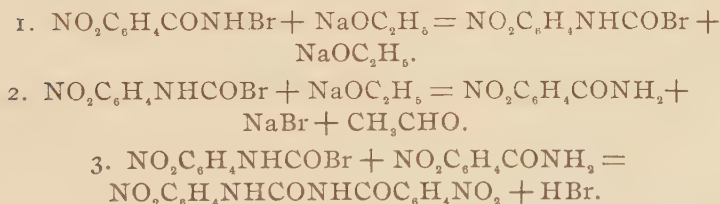
The residue left after extracting with ether was washed to remove the sodium bromide, and the remaining solid dissolved in hot alcohol. On cooling, a reddish brown precipitate was obtained, which after several precipitations, melted at 256° . The crystals are fine needles with a distinct yellow color, insoluble in cold alcohol, ether, ligroin, chloroform, and acetone, and slightly soluble in hot alcohol.

The method of formation suggested, and the analysis proved, this to be symmetrical paranitrophenyl-paranitrobenzoyl urea.

On analysis 0.1203 gram gave 18.8 cc. nitrogen at 742 mm. and 23° .

	Calculated for $\text{C}_{14}\text{H}_{10}\text{N}_4\text{O}_6$.	Found.
Nitrogen	16.98	17.16

It is formed according to the following reactions :



On adding water to the alcoholic solution from which *p*-nitrophenyl-*p*-nitrobenzoyl urea had been separated, crystals were obtained, which were found to be paranitrobenzamide.

The yield was : urethane, 20 per cent. ; amide, 60 per cent. ; urea, 15 per cent.

In greater concentrations (40 grams of absolute alcohol and 1 gram of sodium) no urea was obtained, but a higher per cent. of urethane (30-40), and a lower per cent. of the amide (50-55) resulted. One gram of sodium in 75 grams absolute alcohol gave analogous results. Yield: urethane, 30 per cent. ; amide, 55 per cent. ; urea, 10 per cent.

These results show that sodium ethylate in alcoholic solution acts in a perfectly analogous manner upon benzamide bromide and paranitrobenzamide bromide.

IV. *The Action of Sodium Ethylate on Orthonitrobenzamide Bromide.*

Orthonitrobenzamide bromide was prepared in the same manner as the corresponding para compound, 10.5 grams being added to a solution of one gram of sodium in 40 grams of absolute alcohol carefully cooled. The liquid turned slightly red, and part of the bromide went into solution, but it was necessary to heat on the water-bath to complete the reaction, but for a shorter time than in the case of paranitrobenzamide bromide. At the end of seven minutes the amide bromide had completely disappeared. Acidifying with two drops of dilute acetic acid and cooling, a yellow precipitate was obtained. The alcoholic solution was evaporated to dryness and the residue, together with the precipitate was washed with cold water to remove the sodium bromide. After drying on clay plates, and extracting with ether, ligroïn precipitated from the solution an almost white crystalline body, which melted at 212° . Concentrating the ether-ligroïn solution, and cooling in a freezing-mixture, sulphur yellow crystals were obtained, which dissolved quite readily in warm ligroïn (boiling-point 40° - 60°), and were again precipitated on cooling. These melted at 58° , and appeared to be identical with orthonitrophenyl urethane obtained by Rudolph.¹

To identify it more fully the carbamic ester was synthetically prepared from orthonitraniline and chlorcarbonic ether. The two substances were identical.

The crystals melting at 212° , together with the residue left after extracting with ether, were digested with boiling ether.

¹ Ber. d. chem. Ges., 12, 1295.

After filtering, the cooled filtrate gave an almost white precipitate which, crystallized from acetone, melted at 220° . This substance is difficultly soluble in ether, acetone, benzene and chloroform, but it dissolves readily in hot alcohol from which it is precipitated with difficulty on cooling, but the addition of water causes it to separate out very readily.

The method of formation and analysis show this to be orthonitrophenylorthonitrobenzoyl urea, $\text{NO}_2\text{C}_6\text{H}_4\text{HN}$
 $\text{NO}_2\text{C}_6\text{H}_4\text{CONH} > \text{CO}$.

On analysis 0.2037 gram gave 32 cc. nitrogen at 25° and 741 mm.

	Calculated for $\text{C}_{16}\text{H}_{10}\text{N}_4\text{O}_6$.	Found.
Nitrogen	16.98	17.13

To identify this body more fully, it was synthetically prepared by adding to an ethereal solution of orthonitrophenyl isocyanate the theoretical quantity of orthonitrobenzamide, which immediately yielded a precipitate identical with the above described urea :



From the residue left after digesting with boiling ether, a small amount of orthonitrobenzamide was obtained by extracting with hot alcohol and precipitating by adding water. The yield from the reaction was as follows : urethane, 20 per cent. ; urea, 60 per cent. ; amide, 10 per cent.

A change in concentration of the alcoholic solution modified the relative amounts of the products to a slight extent, but gave no new substances.

One gram of sodium in 50 grams of absolute alcohol, with a molecular quantity of the amide bromide yielded of urethane, 30 per cent. ; of urea, 50 per cent. ; of amide, 10 per cent.

Change in conditions of temperature did not effect the results to any great degree.

IV. *The Action of Sodium Ethylate on Metanitrobenzamide Bromide.*

Metanitrobenzamide bromide was prepared in the same

manner as paranitrobenzamide bromide. 10.5 grams of it were added to 1 gram of sodium in 100 grams of absolute alcohol. Chemical change took place more slowly than in the case of orthonitrobenzamide bromide, since no heat was manifested, and a longer time, 20 minutes, of heating on the water-bath was required to decompose the amide bromide.

During the reaction the odor of acetaldehyde was very strong. The slightly alkaline solution was acidified by a few drops of acetic acid, and freed from alcohol by heating on the water-bath. The residue was extracted with chloroform. From the chloroform solution, ligroïn precipitated metanitrobenzamide (melting-point 141°).

Distilling off the chloroform and ligroïn and taking up the residue with ether, ligroïn precipitated yellow needles which dissolved readily in low-boiling ligroïn (30° – 40°), and were precipitated again on cooling in a freezing-mixture. These melted at 65° .

The method of formation indicated that this was metanitrophenyl urethane. To identify it more fully the carbamate was synthetically prepared from metanitriline and chlorcarbonic ether, and the product thus obtained proved to be identical with that crystallized from ligroïn. Analysis gave the following results:

0.1772 gram gave 21.6 cc. nitrogen at 20° and 743 mm.

	Calculated for $C_9H_{10}N_2O_4$.	Found.
Nitrogen	13.33	13.5

Metanitrophenyl urethane is a yellow substance which crystallizes in fine needles from ligroïn. It is readily soluble in ether, alcohol, chloroform, benzene and acetone. In ligroïn it dissolves more readily than the corresponding ortho or para compounds. It is almost insoluble in water. In alkalies it dissolves with difficulty with slight coloration. Heated in dilute alkalies it saponifies, yielding metanitriline.

The yield was: urethane, 10 per cent.; amide, 80–90 per cent.

A change in the concentration of the alcoholic solution effected a change in both the relative quantities and the kind of products.

1. In quite dilute solutions, 1 gram of sodium in 300 grams of absolute alcohol and 10.5 grams of metanitrobenzamide bromide, the reaction was complete in 15 minutes when heated on the water-bath. The solution was strongly alkaline, and, on adding dilute acetic acid to neutralize, considerable carbon dioxide was given off. On allowing the solution to stand, an almost white crystalline body appeared, which melted at 230° and was identical with metanitrophenylmetanitrobenzoyl urea prepared by O. K. Folin¹ from metanitrophenyl isocyanate and benzamide.

When the alcohol was driven off from the filtrate from which the urea had been obtained, the residue was extracted with ether. From this solution ligroïn precipitated a mixture of metanitrobenzamide and metanitraniline. These were separated by dissolving out the nitraniline with ether in which the amide is very difficultly soluble. The amide was identified by its melting-point, $141^{\circ}.2$, its solubility and general appearance. The metanitraniline melted at 109° . In chloroform solution with dry hydrochloric acid it formed the hydrochloride.

Concentrating the ether-ligroïn solution from which nitraniline and nitrobenzamide had been obtained and cooling to -17° yellow crystals were obtained which melted at 65° , and were identical with the metanitrophenyl urethane previously obtained.

The yield was: urethane, 6 per cent.; amide, 15 per cent.; nitraniline, 55 per cent.; urea, 15 per cent.

2. In very dilute solutions, 1 gram of sodium in 600 grams absolute alcohol, and 10.5 grams of metanitrobenzamide bromide, treated in the same manner as above, no urea was obtained, but other products in the following proportion: Urethane, 6 per cent.; amide, 30 per cent.; nitraniline, 60 per cent.

3. In somewhat concentrated solution, 1 gram of sodium in 60 grams of alcohol there resulted 6 per cent. of urethane and 80-90 per cent. of the amide, and a small quantity of tar. No urea or nitraniline could be found.

4. In more concentrated solutions, 1 gram of sodium in 18

¹ See note, p. 4.

grams of alcohol, the yield was: urethane, traces; amide, 80-90 per cent.; tar, 5-10 per cent.

5. To study the effect of the presence of water when the amide bromide is treated with sodium ethylate, one gram of sodium was added to 60 grams of 98.5 per cent. alcohol, and to the cooled solution were added 10.5 grams of metanitrobenzamide bromide. No more heat was manifested than when the same concentration of absolute alcohol solution was used. The liquid became wine red on heating twenty minutes on the water-bath, when a portion tested with acidified potassium iodide, showed the presence of unchanged amide bromide. The substance then stood in the flask at the temperature of the room over night, when the action was found to be complete. In the flask was found a precipitate of metanitrophenylmetanitrobenzoyl urea. In the filtrate the urethane and amide were found but no nitraniline. The yield was as follows: Urethane, 5-7 per cent.; amide, 25-35 per cent.; urea, 40-50 per cent.

6. In 60 grams of 75 per cent. alcohol the same amounts of amide bromide and sodium ethylate gave only the amide, 80-90 per cent., and tar.

It is evident that the course of the reaction is in principle analogous to that described as taking place when sodium ethylate reacts with benzamide bromide, although the number of products is different. The nitrophenyl urethane, $\text{NO}_2\text{C}_6\text{H}_4\text{-NHCOOC}_2\text{H}_5$, the nitrophenylnitrobenzoyl urea, $\text{NO}_2\text{C}_6\text{H}_4\text{-NHCONHCOC}_6\text{H}_4\text{NO}_2$, and the nitraniline, $\text{NO}_2\text{C}_6\text{H}_4\text{NH}_2$, are all products of the rearrangement of nitrobenzamide bromide $\text{NO}_2\text{C}_6\text{H}_4\text{CONHBr}$. From experiments 1 and 2 it is seen that in very dilute solution a very large amount (60-80 per cent.) of the amide bromide suffered rearrangement, so that in this fundamental manner sodium ethylate in ethyl alcohol acts just as sodium methylate in methyl alcohol,¹ or an aqueous solution of alkalis. The formation of free nitraniline in very dilute solutions is interesting, as it must be due to the saponification of the isocyanate, $\text{NO}_2\text{C}_6\text{H}_4\text{NCO}$, by the alkali, while in concentrated solution where there is less electrolytic dissociation such saponification does not seem to take place to any

¹ Lengfeld and Stieglitz: *Am. Chem. J.*, **15**, 215.

extent. Lengfeld and Stieglitz¹ observed the formation of paranitraniline in an analogous reaction where paranitrobenzamide bromide reacted with dilute sodium methylate in methyl alcohol. In this case in accordance with the stronger electrolytic dissociation of methyl alcohol solutions, the saponification occurs very prominently in a dilution of 1 : 100. The addition of a little water (Ex. 5) to a solution of sodium ethylate, 1 : 60, has the same effect. On increasing the electrolytic dissociation by this means the more concentrated solution gives considerable nitraniline.

V. *The Action of Sodium Ethylate on Succinimide Bromide.*

1. To 40 grams of absolute alcohol 1 gram of sodium was added, and to the cooled solution 8 grams (1 mol.) of well dried succinimide bromide. The sodium became slightly warm and the color changed to reddish brown. Heated twenty minutes on the water-bath the reaction was complete. On neutralizing the slightly alkaline solution with dilute acetic acid, and distilling off the alcohol, there remained a dark brown mass. This was extracted several times with chloroform. On cooling the solution, crystals were obtained which melted at 125° and were identified as succinimide. On concentrating the mother-liquor and adding ligroïn, at first more succinimide was precipitated. This was filtered off. An addition of more ligroïn now precipitated a silver-white, flaky, crystalline body, resembling very strongly in general appearance acetanilide. This recrystallized from ligroïn (boiling-point 30°-40°), melted at 78°. There was obtained less than 5 per cent., nor was the yield increased by repetition of the experiment.

2. On varying the conditions of the experiment the concentration was increased to 1.5 grams of sodium in 40 grams of absolute alcohol, and the molecular quantity of succinimide bromide, on cooling the solution. After the more energetic action had ceased the flask, closed with a calcium chloride tube, stood until succinimide bromide was no longer present in the solution. This took three days. The strongly alkaline solution was acidified with dilute acetic acid, which

¹ Am. Chem. J., 16, 370.

caused carbon dioxide to escape. Treating the contents of the flask as in experiment 1, there resulted almost 5 per cent. of the substance melting at 78° , and 60 per cent. of succinimide.

3. One gram of sodium was added to 40 grams of absolute alcohol and the solution was warmed to 45° when the molecular quantity of succinimide bromide was added in small portions. The action was very energetic, and at the end of ten minutes all the imide bromide had disappeared. The solution was slightly alkaline and when acidified with acetic acid gave off no carbon dioxide. Concentrating and extracting as before about 60 per cent. of succinimide was obtained, together with considerable tar, and less than 3 per cent. of the substance melting at 78° .

Several other conditions of temperature and of dilution of alcoholic solution did not essentially effect the yield. In general there resulted, of succinimide, 50-80 per cent. ; of the substance melting at 78° , 3-5 per cent. ; of tar, 10-30 per cent.

Analysis of the substance melting at 78° showed it to have the composition represented by the formula $C_6H_{10}NO_3$.

I. 0.2098 gram substance gave 18.2 cc. nitrogen at 18° and 746 mm.

II. 0.1827 gram substance gave 16.3 cc. nitrogen at 25° and 743 mm.

III. 0.1642 gram substance gave 0.2970 gram CO_2 and 0.1087 gram H_2O .

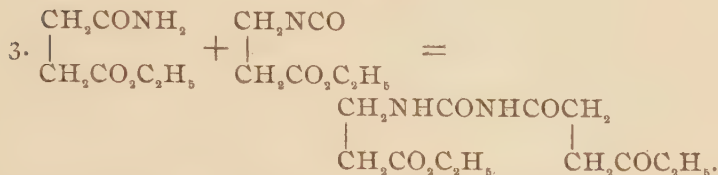
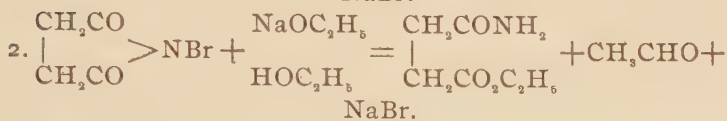
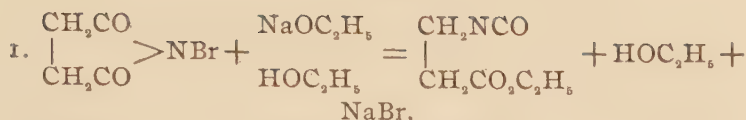
IV. 0.2293 gram substance gave 0.4196 grams CO_2 and 0.1571 gram H_2O .

	Calculated for $C_6H_{10}N_2O_3$.	I.	II.	Found. III.	IV.
Nitrogen	9.72	9.83	9.75		
Carbon	50.00			49.88	49.88
Hydrogen	6.94			7.45	7.35

The method of formation and analysis indicate that this is identical in structure with the dimethyl succinyl- β -ureido-propionate obtained by Lengfeld and Stieglitz,¹ who determined its constitution and molecular weight.

The course of the reaction may be represented by the following equations :

¹ Am. Chem. J., 15, 219.



Diethyl succinyl- β -ureidopropionate is a silver-white substance resembling in appearance acetanilide. It is readily soluble in ether, acetone, alcohol, benzene, and chloroform. It is quite soluble in low-boiling ligroin, from which it may be crystallized by cooling and prolonged stirring.

The formation of the ethyl ester of carboethoxy- β -ureidopropionic acid, corresponding to the methyl ester obtained by Lengfeld and Stieglitz,¹ could not be accomplished.

The action of sodium ethylate in a solution of ethyl alcohol upon amide and amide bromides is twofold. It acts first as a reducing-agent regenerating the acid amide; secondly, as a rearranging-agent changing the amido bromide to a bromformamide or isocyanate. The isocyanate may then react, first, with the alcohol present forming a urethane; second, with the acid amide generated by reduction of the amide bromide forming a symmetrical substituted urea; or, third, it may be saponified, forming the amine. The reaction is perfectly analogous to that of methyl alcoholate in a solution of methyl alcohol or of sodium hydroxide in aqueous solution on acid amide bromides. The products of the chemical change depend upon the concentration of the solution and the kind of amide bromides employed. In very concentrated solutions sodium ethylate acts almost wholly as a reducing-agent regenerating the acid amides. In more dilute solutions rearrangement is effected and urethanes or ureas result. In

¹ Am. Chem. J., 15, 215.

very dilute solutions where the ionization is greater, the isocyanate is saponified and amines are formed.

As a method of forming urethanes the yield is much smaller than when sodium methylate is employed in a solution of methyl alcohol.

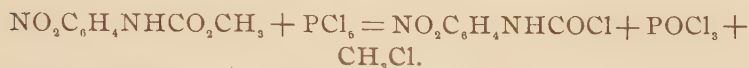
Lengfeld and Stieglitz have ascertained that chlorformanilide and phenyl isocyanate are especially easily obtained from phenyl urethane by the action of phosphorus pentachloride and, since little study has been given to the aromatic isocyanates and few of them have been prepared, the nitrophenyl urethanes obtained in the previous experiments were used to test the general applicability of Lengfeld and Stieglitz's reaction, and to study such chlorformamides and isocyanates.

1. *Chloroform-o-Nitranilide*.—Since the methyl ester of orthonitrocarbanic acid is produced almost quantitatively by the action of sodium methylate in a solution of methyl alcohol it was used instead of the ethyl ester.

In a well dried flask phosphorus pentachloride (7.2 grams) which had been previously washed with sodium-dried ligroin (boiling-point 30° – 40°), and the molecular quantity of methyl-orthonitrophenylurethane, and the two substances were carefully mixed by shaking. No reaction occurred at the ordinary temperature. The flask connected with a long delivery tube, which had been drawn out to a fine point, was heated on the water-bath. At 53° the urethane melted, but no chemical change was manifest. At 59° a few bubbles of gas appeared which became more numerous as the temperature was raised. At 70° the evolution of gas was quite rapid and this temperature was maintained for two hours where no more gas was formed. The escaping gas was identified as methyl chloride burning with a green-tinged flame as it escaped from the tube. On weighing the flask it was found to have decreased in weight 2.2 grams. The theoretical loss of weight for methyl chloride, CH_3Cl , was 1.86 grams. The slight excess may be accounted for by the volatility of the phosphorus oxychloride formed.

The flask now contained a slightly yellow liquid which, extracted with sodium-dried ligroin, gave, when cooled in a freezing-mixture, white needle-shaped crystals, which, on

recrystallizing from the same solvent, melted at 47° . The yield was about 70 per cent. of the theoretical for chloroformanilide, according to the equation



Crystals precipitated from ligroin (boiling-point 20° – 30°) and carefully pressed between filter paper, then allowed to stand twenty minutes in a vacuum-desiccator over vaseline and calcium chloride, gave the following results on analysis :

0.1612 gram heated with lime and precipitated with silver nitrate gave 0.1104 gram AgCl.

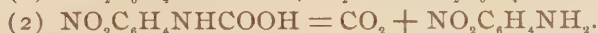
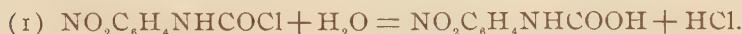
	Calculated for $\text{C}_7\text{H}_5\text{N}_2\text{O}_3\text{Cl}$.	Found.
Chlorine	17.44	16.89

The substance is very difficult to obtain pure for analysis, as it rapidly loses hydrochloric acid. When crystallized from ligroin and dried over vaseline and calcium chloride in a vacuum-desiccator for twelve hours analysis showed a loss of 18 per cent. of the chlorine contained.

0.2172 gram, analyzed as above, gave 0.1246 gram AgCl.

	Calculated for $\text{C}_7\text{H}_5\text{N}_2\text{O}_3\text{Cl}$.	Found.
Chlorine	17.44	14.19

The substance is readily soluble in chloroform, benzene, and ligroin. In water it colors the solution yellow, forming nitraniline (melting-point 71° – 72°) :



With methyl alcohol it forms yellow crystals which melt at 53° , and are identical with the methylorthonitrophenylurethane used as starting material. With ethyl alcohol it forms orthonitrophenylurethane melting at 58° . On standing it loses hydrochloric acid, and on long standing it changes to a white crystalline compound, which melts at 220° , insoluble or nearly so in all organic solvents.

Orthonitrophenylurethane.—The general method of preparing this was devised by Mr. O. K. Folin,¹ as a modification

¹ See note, p. 4.

of the method of Lengfeld and Stieglitz for the preparation of metanitrophenyl isocyanate.

4.45 grams of phosphorus pentachloride, washed with sodium-dried ligroin and the molecular quantity of methyl-orthonitrophenylurethane were heated in a flask for three hours, when no more gas was given off. The loss of weight of the flask was 1.18 grams. The calculated loss of weight in forming the chlorformanilide is 1.13 grams.

The phosphorus oxychloride was then distilled off in a current of dry hydrochloric acid. At the end of three hours the contents of the flask showed no further loss of weight. The loss was 3 grams; calculated loss for phosphorus oxychloride, 3.3 grams. A light-brown liquid remained which was heated in a slow current of dry air at 78° – 80° and then for two hours at 90° , when hydrochloric acid ceased to be given off. There now remained in the flask 3.55 grams of material. The theoretical weight of the isocyanate to be formed was 3.27 grams. On extracting with ligroin almost all went into solution, a small quantity of tar remaining. On cooling the solution an almost white precipitate appeared which, on recrystallization, melted at 41° . The method of formation, analysis, and synthetic products showed the substance to be orthonitrophenyl isocyanate.

I. 0.1616 gram gave 24.3 cc. nitrogen at 15° and 741 mm.

II. 0.3393 gram gave 0.6377 gram CO_2 and 0.0801 gram H_2O .

	Calculated for $\text{C}_7\text{H}_4\text{N}_2\text{O}_3$.	I.	Found. II.
Nitrogen	17.04	17.23	
Carbon	51.27		51.08
Hydrogen	2.44		2.61

Orthonitrophenyl isocyanate, $o\text{-NO}_2\text{C}_6\text{H}_4\text{NCO}$, is an almost white solid melting at 41° . It crystallizes readily from low-boiling ligroin in clusters of delicate needle-shaped crystals. It dissolves readily in chloroform, ether, and benzene. On standing in the air it turns yellow. With water it forms nitraniline. With ethyl and methyl alcohol it gives the corresponding urethanes. On standing twenty days in a vacuum 5 grams changed almost completely into a substance identi-

cal with that formed by long standing of chloroformnitranilide, which is probably the polymeric product, a cyanurate.

A number of derivatives of the isocyanate was prepared.

Isopropyl o-Nitrophenylcarbamate, $o\text{-NO}_2\text{C}_6\text{H}_4\text{NHCO}_2\text{C}_3\text{H}_7$.—To 1 gram of isopropyl alcohol 0.5 gram *o*-nitrophenyl isocyanate was added. The reaction began immediately with evolution of heat. The solution became yellow but no precipitate appeared. On driving off the excess of alcohol there remained a yellow oil, which crystallized after prolonged stirring in a freezing-mixture, but became an oil again at the temperature of the room. The oil dissolved in ligroin, and, on cooling and stirring, crystallized in yellow cubes, which melted at 12° .

0.1606 gram gave 17.8 cc. nitrogen at 19° and 741 mm.

	Calculated for $\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}_4$.	Found.
Nitrogen	12.5	12.47

Isobutyl o-Nitrophenylcarbamate, $o\text{-NO}_2\text{C}_6\text{H}_4\text{NHCO}_2\text{C}_4\text{H}_9$.—When isobutyl alcohol was treated with *o*-nitrophenyl isocyanate in ethereal solution, it yielded yellow crystals, which melted at 13° and were soluble in alcohol and ether, but less soluble in low-boiling ligroin than the corresponding ethyl urethane.

0.1624 gram gave 17.8 cc. nitrogen at 26° and 7.45 mm.

	Calculated for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}_4$.	Found.
Nitrogen	11.76	11.86

Normal Amylo-Nitrophenylcarbamate, $\text{NO}_2\text{C}_6\text{H}_4\text{NHCO}_2\text{C}_6\text{H}_{11}$.—This substance was prepared by adding orthonitrophenyl isocyanate to an excess of normal amyl alcohol, and driving off the excess of alcohol by heating on an oil-bath at 137° . The yellow oil which remained crystallized at -20° and, when precipitated from ligroin, melted at -5° .

0.1960 gram gave 19.8 cc. nitrogen at 21° and 742 mm.

	Calculated for $\text{C}_{12}\text{H}_{16}\text{N}_2\text{O}_4$.	Found.
Nitrogen	11.1	11.26

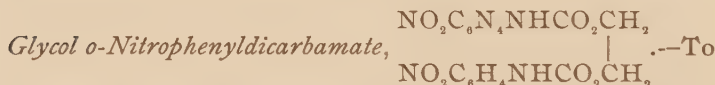
Glycol Nitrophenylmonocarbamate, $o\text{-NO}_2\text{C}_6\text{H}_4\text{NHCO}_2\text{C}_2\text{H}_4\text{OH}$.—To 1 gram of orthonitrophenyl isocyanate in ethereal solu-

tion glycol was added in slight excess of the ratio of 1 molecule of glycol to one of the isocyanate. Repeated shaking during two hours was required to get all the glycol into solution. When the ether was distilled off there remained a yellow oil which, by repeated crystallization from ligroin (boiling-point 20° – 30°), yielded a yellow crystalline body which analyses showed to be glycol orthonitrophenylmonocarbamate.

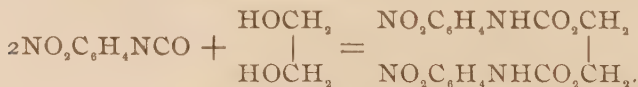
0.1932 gram gave 21.6 cc. nitrogen at 22° and 749 mm.

	Calculated for $C_9H_{10}N_2O_6$.	Found.
Nitrogen	12.39	12.54

Glycol orthonitrophenylmonocarbamate is a yellow crystalline substance which melts at 71° without decomposition. It dissolves readily in ether, alcohol, chloroform, and benzene, but with difficulty in ligroin and water. It is not affected by alkalis or dilute acids in the cold, but when heated they readily decompose it. Its formation is expressed by the equation :



an ethereal solution of 1 gram of *o*-nitrophenyl isocyanate (2 mols.), 1 molecule of glycol was added, and the solution shaken till the glycol dissolved. When the ether was distilled off the yellow oil which remained was heated on the water-bath for twenty minutes to insure complete reaction. Cooled it readily crystallized. Purified by precipitating from ether by ligroin the melting-point remained constant at 160° . The yield is quantitative. Analysis showed the substance to be glycol orthonitrophenyldicarbamate :



0.1335 gram gave 17.5 cc. nitrogen at 24° and 743 mm.

	Calculated for $C_{16}H_{14}N_6O_8$.	Found.
Nitrogen	14.36	14.44

The dicarbamate is a yellow crystalline body melting at 160° . It dissolves with difficulty in ligroin, is quite insoluble in water, but is more soluble in alcohol and ether than the corresponding monocarbamate.

Monoorthonitrocarbanilide, $o\text{-NO}_2\text{C}_6\text{H}_4\text{NHCONHC}_6\text{H}_5$.—When the molecular quantity of aniline dissolved in a few cc. of ether was added to an ethereal solution of *o*-nitrophenyl isocyanate, a precipitate was immediately formed which recrystallized from hot alcohol, melted at 170° . The yield was quantitative.

I. 0.1682 gram gave 0.3737 gram CO_2 and 0.0660 gram H_2O .

II. 0.1848 gram gave 27.4 cc. nitrogen at 23° and 745 mm.

	Calculated for $\text{C}_{13}\text{H}_9\text{N}_3\text{O}_3$.	Found.
Nitrogen	16.37	16.46
Hydrogen	4.28	4.36
Carbon	60.70	60.65

Mono-*o*-nitrocarbanilide is an almost white crystalline substance nearly insoluble in ether, ligroin and cold alcohol, but readily soluble in hot alcohol.

Orthonitrophenylurea, $o\text{-NO}_2\text{C}_6\text{H}_4\text{NHCONH}_2$.—An ethereal solution of one gram of *o*-nitrophenyl isocyanate was saturated with a slow current of dry ammonia. The precipitate which formed immediately was washed with a little ether and recrystallized from hot methyl alcohol when crystals which melted at 181° were obtained.

0.1379 gram gave 28.4 cc. nitrogen at 18° and 744 mm.

	Calculated for $\text{C}_7\text{H}_7\text{N}_3\text{O}_3$.	Found.
Nitrogen	23.21	23.37

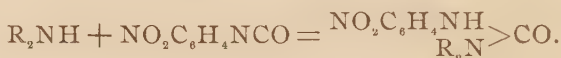
Symmetrical Orthonitrophenylorthotoluy lurea, $\text{NO}_2\text{C}_6\text{H}_4\text{NHCONHC}_6\text{H}_4\text{CH}_3$.—This was obtained by the action of orthotoluidine and *o*-nitrophenyl isocyanate in ethereal solution. Crystallized from alcohol it melts at 189° . In all its properties it closely resembles orthonitrocarbanilide.

0.1989 gram gave 28.6 cc. nitrogen at 26° and 745 mm.

	Calculated for $\text{C}_{14}\text{H}_{13}\text{N}_3\text{O}_3$.	Found.
Nitrogen	15.5	15.75

*The Action of Dialkylated Amines on Orthonitrophenyl
Isocyanates.*

Dialkylated amines are added to *o*-nitrophenyl isocyanate thus :



The character of the reaction is very different from that of the aromatic amines. While the latter form crystalline compounds, in the formation of which chemical action is very energetic ; the former give oils and heating is necessary.

Dimethyl o-Nitrophenylurea, $(CH_3)_2NCONHC_6H_4NO_2$.—Dry dimethylamine was passed into an ethereal solution of *o*-nitrophenyl isocyanate to saturation, but a portion of the solution tested with aniline precipitated orthonitrocarbanilide, showing the presence of unchanged isocyanate. The solution was then warmed and dimethylamine passed into it till a test with aniline gave no precipitate. After the ether was driven off a yellow oil remained which became viscous at -15° and did not crystallize at -30° . This became mobile oil again at 0° . Analysis showed it to be dimethyl-*o*-nitrophenylurea.

0.1140 gram gave 20.7 cc. nitrogen at 23° and 753 mm.

	Calculated for $C_9H_{11}N_3O_3$.	Found.
Nitrogen	20.10	20.38

Diethyl-o-nitrophenylurea, $(C_2H_5)_2NCONHC_6H_4NO_2$.—This was formed by warming an ethereal solution of *o*-nitrophenyl isocyanate and diethylamine. Treating as above described for the corresponding dimethyl compound an oil was obtained which analysis showed to be diethyl-*o*-nitrophenyl urea.

0.1565 gram substance gave 25.4 cc. nitrogen at 23° and 743 mm.

	Calculated for $C_{11}H_{15}N_3O_3$.	Found.
Nitrogen	17.72	17.96

Dipropylorthonitrophenylurea, $(C_3H_7)_2NCOC_6H_4NO_2$, was formed by adding the molecular equivalent of *o*-nitrophenyl isocyanate to an ethereal solution of dipropylamine, except that reaction took place without heating. There is no difference between this and the dimethyl or diethylamine addition-

products. Treated in the same way as above the urea remained as an oil.

0.2000 gram gave 29.1 cc. nitrogen at 25° and 748 mm.

	Calculated for $C_{13}H_{16}N_3O_3$.	Found.
Nitrogen	16.23	16.37

Dibutyl-o-nitrophenylurea, $(C_4H_9)_2NCONHC_6H_4NO_2$.—With *o*-nitrophenyl isocyanate dibutylamine behaved in exactly the same way as dipropylamine, yielding an oil which was prepared as just described.

0.1766 gram gave 23.1 cc. nitrogen at 23° and 748 mm.

	Calculated for $C_{15}H_{23}N_3O_3$.	Found.
Nitrogen	14.43	14.52

Diamyl-o-nitrophenylurea, $(C_5H_{11})_2NCONHC_6H_4NO_2$, was obtained from diamylamine and *o*-nitrophenyl isocyanate. Treated as above described with dipropylamine, perfectly analogous results were obtained. The resulting oil proved to be *diamyl-o-nitrophenylurea*.

0.2259 gram gave 27.4 cc. nitrogen at 25° and 746 mm.

	Calculated for $C_{17}H_{27}N_3O_3$.	Found.
Nitrogen	13.12	13.36

Chlorformparanitranilide, $NO_2C_6H_4NHCOC_6H_5$, was prepared by treating methylparanitrophenylurethane with phosphorus pentachloride in the same manner as the corresponding ortho-nitrophenylurethane. It yielded about 50 per cent. of the urea chloride.

0.2304 gram heated with lime gave 0.1622 gram AgCl.

	Calculated for $C_7H_5N_2O_3$.	Found.
Chlorine	17.46	17.12

Chlorform-p-nitranilide closely resembles chlorformortho-nitranilide. It is almost white with a very penetrating odor, causing tears. With ethyl and methyl alcohol it gives the corresponding urethanes. With ammonia and aniline it gives ureas. Heated above 44° it loses hydrochloric acid slowly and begins to melt. At 75° it loses all its hydrochloric acid and becomes an isocyanate.

Paranitrophenyl Isocyanate, $p\text{-NO}_2\text{C}_6\text{H}_4\text{NCO}$.—10 grams of chlorform- p -nitranilide in a flask with a long delivery tube were heated for 4 hours in a current of dry air at $70^\circ\text{--}75^\circ$. There remained in the flask a brown liquid partially soluble in ligroin, which when cooled, deposited almost white needles in concentric clusters. After two crystallizations they melted at 44° . The substance is p -nitrophenyl isocyanate.

0.1902 gram gave 29.4 cc. nitrogen at 24° and 747 mm.

	Calculated for $\text{C}_7\text{H}_4\text{N}_2\text{O}_3$.	Found.
Nitrogen	17.07	17.12

Water decomposes it giving nitraniline, while amines and alcohols are added to it, forming ureas and urethanes. Standing for a long it polymerizes. Heating hastens polymerization.

Isopropyl- p -nitrophenylurethane, $p\text{-NO}_2\text{C}_6\text{H}_4\text{NHCOC}_3\text{H}_7$, is formed by adding isopropyl alcohol to the molecular quantity of p -nitrophenyl isocyanate. The yield is quantitative. The substance corresponds closely in properties to the methyl and ethyl compounds. It melts at 78° .

0.2293 gram gave 26.1 cc. nitrogen at 24° and 750 mm.

	Calculated for $\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}_4$.	Found.
Nitrogen	12.5	12.66

Isobutyl- p -nitrophenylurethane, $\text{NO}_2\text{C}_6\text{H}_4\text{NHCOC}_4\text{H}_9$ is formed by the direct union of isobutyl alcohol and p -nitrophenyl isocyanate. The yield is quantitative. The substance melts at 62° and has properties analogous to the corresponding propylurethane.

0.2225 gram gave 23.6 cc. nitrogen at 24° and 750 mm.

	Calculated for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}_3$.	Found.
Nitrogen	11.76	11.80

Paranitrocarbanilide, $\text{NO}_2\text{C}_6\text{H}_4\text{NHCONHC}_6\text{H}_5$. — When aniline is added to an ethereal solution of paranitrophenyl isocyanate, a precipitate is formed immediately which melts at 209° and appears to be identical with the substance described by Goldschmidt¹ (melting-point 202°), and by Leuckhart² (melting-point 212°).

¹ Ber. d. chem. Ges., **26**, 2571.

² J. prakt. Chem. **41**, 322.

0.2071 gram gave 30.8 cc. nitrogen at 24° and 741 mm.

	Calculated for $C_{18}H_{11}N_3O_3$.	Found.
Nitrogen	16.34	16.34

In conclusion I desire to express my sincere thanks to Professor Felix Lengfeld for the valuable assistance which he has given me in this work.

